

4121-172

**IN THE CLAIMS:****AMENDMENTS****RECEIVED  
CENTRAL FAX CENTER****JUL 02 2007**

Please amend claim 1 as set forth below.

**Complete Listing of the Claims**

Upon entry of the present amendment, the claims will stand as follows. The following listing of the claims will replace all prior versions and listings of the claims in the present application:

1. (Currently amended) A combination of at least two antibodies, characterized by the following properties:
  - (a) it comprises at least two different multivalent antibodies, each one having at least two specificities, wherein one antibody is and being characterized by features (b) and (d) or and one antibody is characterized by features (b) and (c) as defined below;
  - (b) an antigen-binding domain specific to a tumor antigen;
  - (c) an antigen-binding domain specific to an antigen present on human T-cells; or
  - (d) an antigen-binding domain specific to an antigen present on CD3-epsilon negative human effector cells.
2. (Original) The combination according to claim 1, wherein the tumor antigen is human CD19.
3. (Previously presented) The combination according to claim 2, wherein the CD19 antigen is expressed on human B-cells.
4. (Original) The combination according to claim 1, wherein the tumor antigen is human CD30.
5. (Original) The combination according to claim 4, wherein the CD30 antigen is expressed on human Hodgkin's cells.
6. (Previously presented) The combination according to claim 1, wherein the T-cell antigen is CD3, CD28 or CD5.

4121-172

7. (Previously presented) The combination according to claim 1, wherein the antigen present on CD3-epsilon negative human effector cells is CD16, CD64, CD32 or NKG-2D receptor.
8. (Previously presented) The combination according to claim 7, wherein the antibodies are devoid of constant regions.
9. (Previously presented) The combination according to claim 1, wherein at least two antibodies are multimeric antibodies.
10. (Previously presented) The combination according to claim 1 which comprises single chain Fv-antibodies comprising at least four immunoglobulin variable  $V_H$  and  $V_L$  domains, either separated by peptide linkers or by no linkers.
11. (Previously presented) The combination according to claim 1, which comprises heterodimers of two hybrid single chain Fv-antibodies, each consisting of  $V_H$  and  $V_L$  domains of different specificity against a tumor antigen and an antigen present on CD3-epsilon negative human effector cells or an antigen present on human T-cells, either separated by peptide linkers or by no linkers.
12. (Previously presented) The combination according to claim 1, which comprises homodimers of single chain Fv-antibodies comprising at least four  $V_H$  and  $V_L$  domains of different specificity against a tumor antigen and an antigen present on CD3-epsilon negative human effector cells or an antigen present on human T-cells, either separated by peptide linkers or by no linkers.
13. (Previously presented) The combination of claim 1, wherein said antigen-binding domains mimic or correspond to  $V_H$  and  $V_L$  regions from a natural antibody.
14. (Original) The combination according to claim 13, wherein said natural antibody is a monoclonal antibody, synthetic antibody, or humanized antibody.
15. (Previously presented) The combination according to claim 1, wherein at least one antibody is linked to an effector molecule having a conformation suitable for biological

4121-172

activity or selective binding to a solid support, a biologically active substance, a chemical agent, a peptide, a protein or a drug.

16. (Previously presented) The combination according to claim 1 comprising a third antibody having an antigen-binding domain as defined in (c) or (d) which is different from the antigen-binding domains of the first and second antibody.
17. (Previously presented) The combination of claim 16 comprising a first antibody which is a multivalent multimeric antibody specific to CD19 and CD16, a second antibody which is a multivalent multimeric antibody specific to CD19 and CD3, and, optionally, a third antibody which is specific to CD28.
18. (Previously presented) A polynucleotide encoding a combination of at least two antibodies, characterized by the following properties:
  - (a) it comprises at least two different multivalent antibodies, each one having at least two specificities and being characterized by features (b) and (d) or (b) and (c) as defined below;
  - (b) an antigen-binding domain specific to a tumor antigen;
  - (c) an antigen-binding domain specific to an antigen present on human T-cells; or
  - (d) an antigen-binding domain specific to an antigen present on CD3-epsilon negative human effector cells.
19. (Previously presented) An expression vector comprising the polynucleotide of claim 18.
20. (Original) A host cell containing the expression vector of claim 19.
21. (Previously presented) A process for the preparation of a combination of antibodies according to claim 1, the process comprising:
  - (a) ligating DNA sequences encoding peptide linkers with the DNA sequences encoding the variable domains such that the peptide linkers connect the variable domains resulting in the formation of a DNA sequence encoding a monomer of a multivalent multimeric antibody,

4121-172

(b) expressing the DNA sequences encoding the various monomers in a suitable expression system, and

(c) combining the antibodies.

22. (Previously presented) A composition containing the combination of antibodies according to claim 1.
23. (Original) The composition of claim 22, which is a pharmaceutical composition optionally further comprising a pharmaceutically acceptable carrier or a diagnostic composition optionally further comprising suitable means for detection.
24. (Previously presented) A method for treating B-cell malignancies, B-cell mediated autoimmune diseases or the depletion of B-cells, the method comprising: administering a therapeutically effective amount of a composition according to claim 22.
25. (Previously presented) The method according to claim 24, wherein said B-cell malignancy is non-Hodgkin's lymphoma.
26. (Previously presented) A method for treatment of Hodgkin's disease, the method comprising administering a therapeutically effective amount of the polynucleotides of claim 18.
27. (Previously presented) A gene therapy method for treating B-cell malignancies, B-cell mediated autoimmune diseases or the depletion of B-cells, the method comprising administering a therapeutically effective amount of the expression vector of claim 19.
28. (Previously presented) A method for B-cell malignancies, B-cell mediated autoimmune diseases or the depletion of B-cells, the method comprising: administering a therapeutically effective amount of a composition according to claim 17.

**THE REMAINDER OF THIS PAGE IS INTENTIONALLY LEFT BLANK**